The amendments to the claims do not constitute new matter as defined in 35 U.S.C. § 132. Applicant respectfully requests entry of the amendments and remarks made herein into the file history of the present application.

I. REJECTION OF CLAIMS UNDER 35 U. S. C. § 102

A. REJECTION OF CLAIMS OVER FERREIRA *ET AL.*

On page 3, Paper No. 21, the Examiner maintains the rejection of Claims 1-4, 8-9 and 30-32 under 35 U. S. C. § 102 (b) as allegedly being anticipated by Ferreira *et al.* (WO 97/052258, February 13, 1997) for the same reasons as stated in the Office Action dated August 9, 2002 (Paper No. 18). Specifically, the Examiner contends that Ferreira *et al.*'s peptide, represented by SEQ ID NO: 113, anticipates the peptides of Claim 1, wherein X is any amino acid, X_1 is a fragment thereof containing at least one amino acid and X_2 is zero amino acids.

Additionally, the Examiner contends that Ferreira *et al.*'s SEQ ID NO: 113 "Glu-Ala-Pro-His-Lys-Phe-Lys-Asn-Val" meets the limitations of Claim 2, which requires X_1 and X_2 to be from zero to six amino acids, and limitations of Claims 3-4, which requires X to be Phe, X_1 to be a fragment and X_2 to be two amino acids.

Applicant respectfully traverses the Examiner's rejections for the following reasons.

Claim 30 recites: "A compound of the formula X_1-His-Lys-X-Lys-X_2, wherein X is any amino acid, X_1 is the segment His-Gly-His-Glu-Gln-Gln-His-Gly-Leu-Gly-His-Gly (SEQ ID NO:1) , or N-terminal truncation fragment thereof containing at least one amino acid, and X_2 is (i) zero amino acids, or (ii) the segment Leu-Asp-Asp-Asp-Leu-Glu-His-Gln-Gly-Gly-His-Val (SEQ ID NO:2), or C-terminal truncation fragment thereof containing at least one amino acid, and wherein said compound optionally comprises an amino-terminal protecting group and optionally comprises a carboxy-terminal protecting group."

The Examiner's rejection of Claim 30 is based on an incorrect interpretation of the language "N-terminal truncation fragment" of His-Gly-His-Glu-Gln-Gln-His-Gly-Leu-Gly-His-Gly (SEQ ID NO:1) "containing at least one amino acid." According to the Examiner, the language "N-terminal truncation fragment" refers to an X_1 peptide that may lack any of the cited X_1 amino acids, so long as one amino acid of X_1 is retained. The Examiner insists that the one amino acid retained can be any amino acid from SEQ ID NO:1. Applicant respectfully disagrees.

Applicant respectfully submits that the Examiner's interpretation of the claimed language "N-terminal truncation fragment...containing at least one amino acid" is against the spirit and intended scope of the claimed invention.

Applicant submits for the record that "N-terminal truncation" means, as the term suggests, removing one or more contiguous amino acids beginning from the N-terminus of SEQ ID NO:1, not randomly removing amino acids anywhere from within SEQ ID NO:1 as the Examiner suggests. In other words, peptides having an X_1 wherein one or more amino acids are removed randomly from different parts of SEQ ID NO:1 do not fall within the intended scope of the invention, and would not infringe this claim.

As the Examiner is no doubt aware, the claims, specification and prosecution history of an application ensure that the scope of the claims is clear so that the public is informed of the boundaries of what constitutes infringement of the patent. In the case at hand, the specification, claims and prosecution history have provided more than abundant notice to the public that Applicant is <u>not</u> claiming a peptide wherein random, non- contiguous deletions can be made in SEQ ID NO:1.

Applicant's response to the Office Action dated August 9, 2002 (Paper No. 18) provided two tables (Table 1 and 2) that demonstrated amino acid sequences of the N-terminal and C-terminal truncated fragments of the claimed invention, respectively. These tables schematically show the scope of the N-terminal and C-terminal peptide fragments claimed and therefore, demonstrate the scope and intended meaning of the language "N-terminal truncation fragment" and "C-terminal truncation fragment" "containing at least one amino acid" in the specification and claims of this application. All truncation possibilities within the scope of the invention

claimed were presented in these tables. The N-terminal and C-terminal truncations clearly show that peptides having random removal of amino acids from within SEQ ID NO:1 are not encompassed within the peptides claimed. For the ease of analysis, these tables are reproduced below.

Examiner's interpretation of "N-terminal truncation fragment" and "N-terminal truncation fragment" are inconsistent with the plain meaning of the words. "N-terminal" refers to the "*end* of a peptide that carries the amino acid that has a free alpha amino group". Likewise, "C-terminal" refers to the "*end* of a peptide that carries the amino acid that has a free alpha carboxyl group". *Dictionary of Biochemistry and Molecular Biology*, John Wiley & Sons, New York, NY, 2nd ed. 1998, pages 110 and 328 (Exhibit C). Prominent in these definitions is the word "*end*". Similarly, the word "truncate" means "to shorten by or as if by cutting *off*". *Webster's New Collegiate Dictionary,* G. & C. Meriam Co., Springfield, MA, 1977, p. 1255 (Exhibit D). Clearly, a thing can be shortened by "cutting off" only if that cutting takes place from an end, not from an interior part of the thing. The latter would be "cutting out", not *cutting off*, and is inconsistent with the standard dictionary definition of the verb *truncate*. Clearly, the only reasonable interpretation of the claim language "N-terminal truncation fragment" and "C-terminal truncation fragment" is a fragment generated by the removal of one or more contiguous amino acids from the *end* of a peptide.

Table 1 - TRUNCATION POSSIBILITIES OF N-TERMINAL

→ His-Gly-His-Glu-Gln-Gln-His-Gly-Leu-Gly-His-Gly

Gly-His-Glu-Gln-Gln-His-Gly-Leu-Gly-His-Gly

His-Glu-Gln-Gln-His-Gly-Leu-Gly-His-Gly

Glu-Gln-Gln-His-Gly-Leu-Gly-His-Gly

Gln-Gln-His-Gly-Leu-Gly-His-Gly

Gln-His-Gly-Leu-Gly-His-Gly

His-Gly-Leu-Gly-His-Gly

Gly-Leu-Gly-His-Gly

Leu-Gly-His-Gly

Gly-His-Gly

Gly

Table 1 shows that smallest N-terminal truncation fragment of SEQ ID NO:1 is the amino acid Gly. It is respectfully submitted that truncating SEQ ID NO:1 from the N-terminus to the maximum extent possible, *i.e.*, leaving only one original amino acid of SEQ ID NO:1, results in the single amino acid Glycine (Gly) as X_1. Thus, the claimed peptide is characterized by the minimal sequence **Gly**-His-Lys-X-Lys. Accordingly, Ferreira *et al*'s peptide Glu-Ala-Pro-His-Lys-Phe-Lys-Asn-Val does not anticipate the peptide of the invention as claimed.

Claims 1 and 30 are not anticipated by the Glu-Ala-Pro-His-Lys-Phe-Lys-Asn-Val (as SEQ ID NO:113) peptide of Ferreira *et al.* for yet another reason. X_2 in Applicant's X_1-His-Lys-X-Lys-X_2 peptide is (i) zero amino acids, (ii) the specific 12-amino acid sequence SEQ ID NO:2, or (ii) a C-terminal truncation fragment of Leu-Asp-Asp-Asp-Leu-Glu-His-Gln-Gly-Gly-His-Val (SEQ ID NO:2) containing at least one amino acid. The C-terminal truncation fragments within the scope of the claims are generated by a truncation operation which starts at the C-terminal end of SEQ ID NO:2 and proceeds contiguously in the N-terminal direction removing one, two, three, etc. amino acids until one amino acid remains. All truncation possibilities encompassed within the scope of the C-truncated peptides of the claimed invention are thus represented by the set of sequences of Table 2:

Table 2 - TRUNCATION POSSIBILITIES OF C-TERMINAL

Leu-Asp-Asp-Asp-Leu-Glu-His-Gln-Gly-Gly-His-Val←

Leu-Asp-Asp-Asp-Leu-Glu-His-Gln-Gly-Gly-His

Leu-Asp-Asp-Asp-Leu-Glu-His-Gln-Gly-Gly

Leu-Asp-Asp-Asp-Leu-Glu-His-Gln-Gly

Leu-Asp-Asp-Asp-Leu-Glu-His-Gln

Leu-Asp-Asp-Asp-Leu-Glu-His

Leu-Asp-Asp-Asp-Leu-Glu

Leu-Asp-Asp-Asp-Leu

Leu-Asp-Asp-Asp

Leu-Asp-Asp

Leu-Asp

Leu

To correspond to Ferreira *et al.*'s nonapeptide, Applicant's X_2 must be two amino acids. But it is clear from Table 2 that when X_2 is two amino acids in the claimed peptides, that two-amino acid sequence must be **Leu-Asp**. The corresponding two-amino acid sequence in the Ferreira nonapeptide is ***Asn-Val***. Similarly, for Applicant's X_1 to correspond to Ferreira's nonapeptide, Applicant's X_1 must consist of three amino acids. From Table 1, the three-amino acid sequence in the claimed peptides must be ***Gly-His-Gly***. The corresponding three-amino acid sequence in the Ferreira nonapeptide is **Glu-Ala-Pro**. The resulting claimed and Ferreira peptides are thus compared as follows:

Claimed	Gly-His-Gly-His-Lys- X -Lys-Leu-Asp
Ferreira *et al.*	Glu-Ala-Pro-His-Lys-Phe-Lys-Asn-Val

Thus, it should be abundantly clear from the foregoing that Ferreira does not anticipate Claims 1-4, 8-9 and 30-32. Reconsideration and withdrawal of the Section 102 rejection is respectfully requested.

B. REJECTION OF CLAIMS OVER JP07092171

On page 3, Paper No. 21, the Examiner rejects Claims 1 and 35 under 35 U. S. C. § 102(b) as allegedly being anticipated by (FARH) HOECHST JAPAN, Accession Number AAR75186, JP07082172-A 1995, (hereinafter, "JP07082172"). Specifically, the Examiner contends that JP07092171 discloses a formula wherein X is any amino acid, X_1 is a fragment thereof containing at least one amino acid and X_2 is zero amino acids. The Examiner believes that the JP07082172 formula encompasses the basic sequence "Gly-His-Lys-X-Lys" of the claimed invention. Additionally, the Examiner contends that JP07092171 discloses a compound that is 100% identical to the compounds claimed, as set forth in SEQ ID NO: 9 of this application. The Examiner alleges that because the claims recite the open language "having" or "comprising," the elements of the claims are met by the reference, even though the reference compound is longer than the claimed polypeptides. Applicant traverses the Examiner's rejections for the following reasons.

Claim 1 defines a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound of the formula X_1-His-Lys-X-Lys-X_2, wherein X is one amino acid, and X_1 and X_2 are each up to a maximum of twelve defined amino acids. The largest peptide within the scope of claim 1 is therefore the 28-amino acid peptide SEQ ID NO:1-His-Lys-X-Lys-SEQ ID NO:2.

It is respectfully submitted that the anticipation rejection is based upon a misreading of claim 1. The formula X_1-His-Lys-X-Lys-X_2 is not open-ended in the sense that Examiner is free to disregard the size limitation inherent in the formula. While the open-ended transition word "comprising" is present, the word appears in the preamble of the claim, linking the two elements of the claimed pharmaceutical composition - "a pharmaceutically acceptable carrier" and "a compound of the formula X_1-His-Lys-X-Lys-X_2". The "comprising" preamble word opens the claimed composition to other ingredients in the pharmaceutical composition. The "comprising" word does not serve to enlarge the clear boundaries of the formula X_1-His-Lys-X-Lys-X_2.

Examiner alleges that the word "having" somehow opens claim 1 to an interpretation that embraces JP07082172. The word "having" does not even appear in claim 1.

Moreover, the peptides contained in the composition of Claim 1, as discussed above, require the minimal sequence **Gly**-His-Lys-X-Lys. The general formula of JP07082172 disclosing a formula wherein X is any amino acid, X_1 is a fragment thereof containing at least one amino acid, and X_2 is zero does not teach or suggest the peptide of Claim 1.

Applicant respectfully submits that JP07092171 does not teach or suggest the compound of Claim 35 (SEQ ID NO: 9). The Examiner contends that this reference discloses a compound that is 100% identical to the compound represented by SEQ ID NO: 9 of this application. Applicant was unable to find such compound in the disclosure and sequence listing of JP07092171. Applicant requests the Examiner to indicate where exactly in the disclosure of JP07092171 such compound is disclosed.

Claim 35 is directed to a 16-amino acid peptide represented by SEQ ID NO:9. For a reference to anticipate this claim, it must disclose the SEQ ID NO:9 peptide. JP07092171 is not such reference. Applicant respectfully submits that the transitional phrase "having" in a claim directed to a peptide represented by a specific amino acid sequence does not in any way subject the claim to anticipation by a reference that does not disclose that peptide.

Nevertheless, without acquiescing in the propriety of the Examiner's proposed amendment, and solely to advance prosecution of this application, Applicant has amended Claim 35 to substitute the term "having" with the transitional phrase "consisting essentially of".

In view of the forgoing remarks and the amendment to Claim 35, reconsideration and withdrawal of this rejection is respectfully requested.

C. REJECTION OF CLAIMS OVER JP08208692

On page 4, Paper No. 21, the Examiner rejects Claim 34 under 35 U. S. C. § 102(b) as allegedly being anticipated by (SUMU) SUMITOMO SEIYAKU KK, Accession Number AAW07625, JP08208692-A, 1996 (hereinafter, "JP08208692). Specifically, the Examiner

contends that JP08208692 teaches a compound that is 100% identical to the compound claimed and set forth in SEQ ID NO: 8 of the instant specification. The Examiner believes that because the claim contains the transitional work "having", the claim is met by the reference, even though the compound disclosed by the reference is longer than the claimed compound. Applicant respectfully traverses the Examiner's rejection.

Applicant respectfully submits that JP08208692 does not teach or suggest the compound of Claim 34 (SEQ ID NO: 8). Applicant was unable to find such compound in the disclosure and sequence listing of JP08208692. Applicant requests the Examiner to indicate where exactly in the disclosure of JP08208692 such compound is disclosed.

Claim 34 is directed to a 16-amino acid peptide represented by SEQ ID NO:8. For a reference to anticipate this claim, it must disclose that peptide. JP08208692 is not such reference. Applicant respectfully submits that the transitional phrase "having" in a claim directed to a peptide represented by a specific amino acid sequence does not in any way subject the claim to anticipation by a reference that does not disclose that peptide.

Nevertheless, without acquiescing in the propriety of the Examiner's proposed amendment, and solely to advance prosecution of this application, Applicant has amended Claim 34 to substitute the term "having" with the transitional phrase "consisting essentially of."

In view of the amendment to Claim 34, reconsideration and withdrawal of this rejection is respectfully requested.

II. ART OF RECORD

The Examiner states that JP07082172 is made of record and is considered pertinent to the method claims. Specifically, the Examiner states that JP07082172 allegedly teaches the sequence set forth in SEQ ID NOS: 5 and 7 which are recited in the method claims. The Examiner notes that this abstract does not explicitly teach a method of inhibition of angiogenesis, but discloses sequences that correspond to a human kininogen useful in wound healing.

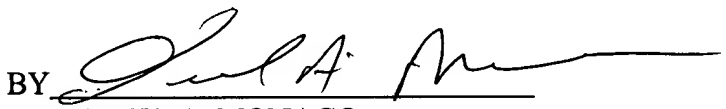
Applicant agrees that JP07082172 does not disclose a method for inhibiting angiogenesis. Applicant disagrees, however, that the claimed compounds represented by SEQ ID Nos: 5 and 7 are disclosed in the reference.

CONCLUSION

In light of the above, Applicant respectfully submits that all pending claims are allowable over the art of record, and a Notice of Allowance is courteously solicited. The foregoing is submitted as a full and complete response to the Office Action mailed March 26, 2003 (Paper No. 3). The Examiner is invited and encouraged to contact the undersigned attorney of record if such contact will facilitate an efficient examination and allowance of the application.

Respectfully submitted,

KEITH R. MCRAE

BY 

DANIEL A. MONACO
Registration No. 30,480
DRINKER, BIDDLE & REATH, LLP.
One Logan Square
18th and Cherry Streets
Philadelphia, PA 19103
(215) 988-3312 ph.
(215) 988-2757 fax
Attorney for Applicant